CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-986

MICROBIOLOGY REVIEW(S)

FEB - 8 1999

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF NDA 20-986
4 February 1999

A. 1. NDA 20-986 BI
APPLICANT: Novo Nordisk Pharmaceuticals, Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

2. PRODUCT NAME: Insulin Aspart (Insulin X-14) Injection (recombinant DNA origin)

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is a sterile injectable preparation for subcutaneous injection.

4. METHODS OF STERILIZATION:
The product is ———

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is indicated in the treatment of diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: 29 January 1999 (Subject of this Review)

3. RELATED DOCUMENTS: IND ——; NDA 19-938; DMF —
DMF —; DMF ——

4. ASSIGNED FOR REVIEW: 30 September 1998

C. REMARKS: The product will be manufactured by:

Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
Denmark

The product is to be packaged in the following presentations:

10 mL vial

PenFill® 3 mL cartridge

Prefilled® 3 mL syringe

It is the applicant's intent to market only the 10mL vial, Penfill® 3mL cartridge, and Prefilled® 3mL syringe at the present time. Should Novo Nordisk decide the other presentations, labeling will be submitted to the Agency for review.

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

/S/ 4 February 1999
Paul Stinavage, Ph.D.
/S/ 2/8/99

cc: Original NDA 20-986
HFD-510/J. Rhee/Div. File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 February 1999
R/D initialed by P. Cooney

APPEARS THIS WAY
ON ORIGINAL

FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION 2/3/99

TO (Division Office): Paul Stinavage, Ph.D., HFD-160			FROM: HFD-510 (Division of Metabolic and Endocrine Drug Products) Julie Rhee	
E bruary 3, 1999	IND NO.:	NDA NO.: 20-986	TYPE OF DOCUMENT: Microbiology response	DATE OF DOCUMENT: January 29, 1999
NAME OF DRUG: Insulin Aspart (insulin X-14 [rDNA])	PRIORITY CONSIDERATION:		CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE: March 15, 1999

NAME OF FIRM: Novo Nordisk

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE–NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ■ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW THER	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

/S/ /S/ 2/3/99

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

CENTER FOR DRUG EVALUATION AND RESEARCH RECD FEB 3 HFD-160

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Paul, this is Novo's response to your earlier requests. For your information, a copy of the fax that was sent to Novo is attached. Thank you.

cc: Original NDA 20-986
HFD-510/Div. Files

SIGNATURE OF REQUESTER: /S/	METHOD OF DELIVERY (Check one): ☐ MAIL ☒ HAND
SIGNATURE OF RECEIVER: /S/ 2-3-99	SIGNATURE OF DELIVERER: /S/ 2-3-99

JAN - 4 1999

REVIEW FOR HFD-510
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW OF NDA 20-986
4 January 1999

A. 1. NDA 20-986
APPLICANT: Novo Nordisk Pharmaceuticals, Inc.
Suite 200
100 Overlook Center
Princeton, NJ 08540-7810

2. PRODUCT NAME: Insulin Aspart (Insulin X-14) Injection (recombinant DNA origin)

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4. METHODS OF STERILIZATION:
The product is ———

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The drug product is indicated in the treatment of diabetes mellitus.

B. 1. DATE OF INITIAL SUBMISSION: 16 September 1998

2. DATE OF AMENDMENT: (none)

3. RELATED DOCUMENTS: IND —— ; NDA 19-938; DMF ——
DMF —— DMF ——

4. ASSIGNED FOR REVIEW: 30 September 1998

C. REMARKS: The product will be manufactured by:

Novo Nordisk A/S
Novo Alle
DK-2880 Bagsvaerd
Denmark

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10 mL vial

PenFill® 3 mL cartridge

Prefilled® 3 mL syringe

It is the applicant's intent to market only the 10mL vial, Penfill® 3mL cartridge, and Prefilled® 3mL syringe at the present time. Should Novo Nordisk decide the other presentations, labeling will be submitted to the Agency for review.

D. CONCLUSIONS: The application is approvable pending resolution of microbiology concerns.

/S/ 4 January 1999
Paul Stinavage, Ph.D.
/S/ 1/4/99

cc: Original NDA 20-986
HFD-510/J. Rhee/Div. File
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 4 January 1999
R/D initialed by P. Cooney

APPEARS THIS WAY
ON ORIGINAL

FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO (Division/Office):	FROM:
HFD-805 Microbiology Peter Cooney	HFD-510 (Division of Metabolic and Endocrine Drug Products) 9/23/98

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
September 23, 1998		20-986		Sept 16, 1998

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Insulin Aspart X-14	STANDARD		July 30, 1999

NAME OF FIRM: Novo Nordisk Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
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- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
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- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER (SPECIFY BELOW): Micro

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

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- ☐ BIOAVAILABILITY STUDIES
- ☐ PHASE IV STUDIES
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- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISION RICK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ [illegible]

COMMENTS/SPECIAL INSTRUCTIONS:

(Project Manager 7-6424)

To: P. Stravage

/S/ 9/30/98

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP 24 1998
HFD-160

SIGNATURE OF REQUESTER /S/ for Julia Rhee 9/23/98	METHOD OF DELIVERY (Check one) ☒ MAIL ☐ HAND
NATURE OF RECEIVER /S/	SIGNATURE OF DELIVERER